S221 Gene Therapy for Cystic Fibrosis: Where Do We Stand

E.W.F.W. Alton. *Ion Transport Unit, National Heart & Lung Institute, London, United Kingdom*

The cystic fibrosis (CF) gene was cloned was in 1989, and the feasibility of *in vitro* gene therapy demonstrated by 1991. With the development of CF mouse models, two groups demonstrated that CFTR gene transfer is able to correct, at least in part, the bioelectrical abnormality characteristic of CF. As a result of these and other studies, CF gene therapy has moved into the clinical arena. Currently, 4 clinical trials have been reported with at least another dozen underway or recently completed. The preliminary data available from these studies suggests that both adenoviral and cationic liposome mediated gene transfer can be demonstrated at the level of both mRNA and protein. With respect to functional correction, approximately 30% of subjects studied have demonstrated evidence of some degree of correction of the chloride abnormality characteristic of CF. A number of safety issues have arisen with regard to adenoviral mediated gene transfer, whilst to date liposomes have proved to be safe. The data from these studies will be reviewed in this presentation.

S222 Congenital Immuno-Deficiency

C. Bordignon. *I*

No abstract available.

Latest lessons from experimental models (ESCMID European Network for the Study of Experimental Infections)

S223 Molecular Mediators of Brain Injury in Experimental Meningitis

M.G. Täuber. *CH*

No abstract available.

S224 Latest Lessons from Experimental Models

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Objectives: Animal models have been traditionally used to evaluate the pathogenesis of infectious diseases or to investigate the safety, pharmacokinetics, pharmacodynamics and/or efficacy of antimicrobials. From these models, parameters of antibiotic use have evolved and have helped in the management of specific diseases like meningitis or endocarditis. Recently some antibiotics have been shown to modulate host response. Appropriately designed, experimental models may become powerful tools to explore not only the *in vivo* antimicrobial activity of antibiotics but their Biological Response Modifiers (BRM) properties.

Methods: A murine model of pneumococcal pneumonia was developed i) to study the chronology of events which mediates the progression of the inflammatory response and leads to death, ii) to detect specific markers of disease progression, and iii) to evaluate how antibiotics can interact with the immune system and control this deadly infection.

Results: There was no correlation between the kinetics of cytokines in blood and that observed in bronchoalveolar fluid (BAL) or lung. The simultaneous elevation of IL-6 and TNF observed in blood may be a sign of poor prognosis and imminent death, while high level of IL-6 may suggest early disease with limited lung damage. In this model, cefodizime (Cef) did reduce the level of LTB_4 and neutrophil recruitments in the lungs of infected animals. Moreover, this β-lactam did selectively inhibit TNF and IL-6 in BAL and lung tissue without altering IL-1 production. By reducing the overwhelming inflammatory response that occurs during severe pneumonia, this antibiotic may protect the host in unique ways.

Conclusions: Animal studies based at developing strategies of immune modulation may eventually lead to therapies of unparalleled efficacy and safety.

S225 Understanding Host Defence Mechanisms by Gene Manipulation

J.Y. Cesbron. *F*

No abstract available.

S226 Pneumonia: News from the Experimental Models

W.R. Wilson. *USA*

No abstract available.

Evolving natural history and prognostic factors in febrile neutropenia (ESCMID Working Party on Infections in Cancer Patients)

S227 Evolving Natural History and Prognostic Factors in Febrile Neutropenia

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Since December 1994, the Infectious Committee of the Multinational Association for Supportive Care in Cancer (MASCC) is conducting a survey, in a multicentric, multinational setting among febrile neutropenic cancer patients (pts) in order to identify features at presentation able to predict a good outcome or the occurrence of a serious medical complication with a particular interest in an external validation of the prediction rule published by Talcott in JCO (1992) where pts are allocated into 4 groups: I: inpts, II: outpts with comorbidity, III: outpts with uncontrolled cancer, IV: outpts without comorbidity or uncontrolled cancer. Up to January 31, 1997, about 900 eligible pts have been followed for one episode. Interim descriptive results currently available are the following: median age is 52 yrs with 49% of male pts. Underlying disease was hematologic in 46%, lymphoma/Hodgkin's disease in 20%, solid tumor in 26% and other in 9%; 23% did undergo a transplantation. A clinical site was found in 42% and Talcott's group distribution was: I:62%, II:13%, III:9% and IV:16%. Initial empiric antibiotic treatment was successful in 55%, a serious medical complication occurred in 17% with a 7% death rate. Closure of the survey will occur soon, after 1000 episodes and definitive results including inferential analysis will be available at the meeting.